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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/229,173	01/13/1999	DEB K. CHATTERJEE	0942.2800008	7438

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EXAMINER

HUTSON, RICHARD G

ART UNIT PAPER NUMBER

1652

DATE MAILED: 11/10/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Advisory Action	Application No. 09/229,173	Applicant(s) CHATTERJEE, DEB K.	
	Examiner Richard G Hutson	Art Unit 1652	

--The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

THE REPLY FILED 09 October 2003 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE. Therefore, further action by the applicant is required to avoid abandonment of this application. A proper reply to a final rejection under 37 CFR 1.113 may only be either: (1) a timely filed amendment which places the application in condition for allowance; (2) a timely filed Notice of Appeal (with appeal fee); or (3) a timely filed Request for Continued Examination (RCE) in compliance with 37 CFR 1.114.

PERIOD FOR REPLY [check either a) or b)]

- a) ☐ The period for reply expires _____ months from the mailing date of the final rejection.
- b) ☐ The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection. ONLY CHECK THIS BOX WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

1. ☒ A Notice of Appeal was filed on 10/9/2003. Appellant's Brief must be filed within the period set forth in 37 CFR 1.192(a), or any extension thereof (37 CFR 1.191(d)), to avoid dismissal of the appeal.
2. ☐ The proposed amendment(s) will not be entered because:
- (a) ☐ they raise new issues that would require further consideration and/or search (see NOTE below);
 - (b) ☐ they raise the issue of new matter (see Note below);
 - (c) ☐ they are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or
 - (d) ☐ they present additional claims without canceling a corresponding number of finally rejected claims.

NOTE: _____.

3. ☒ Applicant's reply has overcome the following rejection(s): See Continuation Sheet.
4. ☐ Newly proposed or amended claim(s) _____ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).
5. ☒ The a) ☐ affidavit, b) ☐ exhibit, or c) ☒ request for reconsideration has been considered but does NOT place the application in condition for allowance because: See Continuation Sheet.
6. ☐ The affidavit or exhibit will NOT be considered because it is not directed SOLELY to issues which were newly raised by the Examiner in the final rejection.
7. ☐ For purposes of Appeal, the proposed amendment(s) a) ☐ will not be entered or b) ☐ will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.

The status of the claim(s) is (or will be) as follows:

Claim(s) allowed: 38 and 40-44.

Claim(s) objected to: _____.

Claim(s) rejected: 1,3,5-10,13,16,17,19,26,28,29 and 34-37.

Claim(s) withdrawn from consideration: _____.

8. ☐ The proposed drawing correction filed on _____ is a) ☐ approved or b) ☐ disapproved by the Examiner.
9. ☒ Note the attached Information Disclosure Statement(s) (PTO-1449) Paper No(s). 11/01, 10/03.
10. ☒ Other: See Continuation Sheet



Richard G Hutson, Ph.D.
Primary Examiner
Art Unit: 1652

Continuation of 3. Applicant's reply has overcome the following rejection(s): Applicants amendment has overcome the previous 112 second paragraph rejection of claim 1. The rejection of claim 1 (3, 5-10, 13, 16, 17, 19, 26, 28, 29, 34-37 dependent from) as being indefinite in that the metes and bounds of what applicants considers to be the "3'-5' exonuclease domain" and the "5'-3' exonuclease domain" of the claimed mutant *Thermotoga maritima* DNA polymerase mutants is hereby withdrawn based on applicants previous argument that Gelfand et al. teach that the "3'-5' exonuclease domain" (See Gelfand et al., U.S. Patent No. 5,374,553) of Tma DNA polymerase is defined by amino acids 291 through 484 (See column 7, lines 16-34 and column 13, lines 51-53). Gelfand et al. further teach that the 5'-3' exonuclease domain of Taq DNA polymerase corresponds to amino acids 1-289 of Taq DNA polymerase. This corresponds to a 5'-3' exonuclease domain of Tma DNA polymerase which comprises amino acids 1-291..

Continuation of 5. does NOT place the application in condition for allowance because:
Claims 1, 3, 5-10, 13, 16, 17, 19, 26, 28, 29 and 34-37 remain rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1, 3, 5-10, 13, 16, 17, 19, 26, 28, 29 and 34-37 remain indefinite in that the recitation "...wherein said mutation is selected from th group consisting of: a deletion, a single or double substitution, a frame shift mutation and an insertion" is unclear. As previously stated, the inclusion of frame shift mutations in the group of sought mutations is unclear as frame shift mutations would result in the not only the potential loss of 5'-3' exonuclease activity, 3'-5' exonuclease activity and discriminatory behavior against dideoxynucleotides, but the loss in polymerase activity itself, as presumably any domain which follows the frame shift, as one would read amino-terminal to carboxyl-terminal, would be lost. As the polymerase domain is on the carboxyl terminal side of each of the specifically referred to domains, any frameshift that would result in loss of exonuclease activity would also result in a loss in polymerase activity.

In response to this rejection, applicants argue that a frameshift mutation would not necessarily lead to the loss of activity of the claimed DNA polymerase as applicants submit that a frameshift mutation near the end of the carboxyl-terminal domain would not lead to any loss of 5'-3' exonuclease activity, 3'-5' exonuclease activity, discriminatory behavior against dideoxynucleotides, or polymerase activity. This argument is not found persuasive as it is unclear. Applicants are reminded that the current claims are drawn to a Tma DNA polymerase which comprises a mutation in the 3'-5' exonuclease domain, the 5'-3' exonuclease domain or the O-helix of said polymerase, and any frameshift mutation would alter the activity of any domain that is located toward the carboxyl end of where the frameshift occurs. Thus a frameshift mutation in any of the 3'-5' exonuclease domain, the 5'-3' exonuclease domain or the O-helix domain would by definition effect the polymerase domain. Further still applicants are reminded that by definition the referred to mutations (i.e. frameshift mutations) must "reduce or eliminate" either the 5'-3' exonuclease activity, 3'-5' exonuclease activity or the discriminatory behavior against dideoxynucleotides.

Claims 1, 3, 5-8, 10, 13, 16, 17, 19, 26, 28, 29 and 34-37 remain rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

This rejection is stated in the previous office actions, Paper No. 12, 11/21/2000, Paper No. 15, 7/30/2001, Paper No. 26, 5/1/2002 and Paper No. 32, 4/7/2003 and applicants traversals are found in Paper No. 14, 5/21/2001, Paper No. 20, 12/18/2001, Paper No. 26, 5/1/2002 and Paper No. 31, 1/8/2003.

In response to this rejection applicants have amended claims 1 and 37 to indicate that "said [mutant] *Thermotoga maritima* (Tma) DNA polymerase has a molecular weight of about 100 kilodaltons" and refer to the previous responses filed on 5/21/2001, 12/18/2001 and 1/8/2003. Applicants further submit that the additional structural information regarding the size of the resultant Tma DNA polymerase mutants (i.e. approximately 100 kd) should necessitate the withdrawal of this rejection. Applicants argument is not found persuasive for the reasons previously stated in response to applicants submissions on 5/21/2001, 12/18/2001 and 1/8/2003. In response to applicants amendment of the claimed mutant Tma DNA polymerases to a size of 100 kilodaltons, this is not found persuasive for the reasons previously stated, and because applicants amendment while more descriptively defining the claimed genus structurally, does not more descriptively define the type of mutations claimed structurally. It remains that encompassed within the claimed genus is "any mutation with the specified effect" or those types of mutations which taken as a whole equate to any mutation with the specified effect.

Applicant is referred to the revised guidelines concerning compliance with the written description requirement of U.S.C. 112, first paragraph, published in the Official Gazette and also available at www.uspto.gov..